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CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC
1420 FIFTH AVENUE
SUITE 2800
SEATTLE, WA 98101-2347

EXAMINER	
NEGIN, RUSSELL SCOTT	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/764,420	LUM ET AL.	
	Examiner	Art Unit	
	Russell S. Negin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33 and 68-70* is/are pending in the application.

4a) Of the above claim(s) *5-7,10 and 11* is/are withdrawn from consideration.

5)☒ Claim(s) *33* is/are allowed.

6)☒ Claim(s) *1-4,8,9,12-32 and 68-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Comments

Applicants' request for reconsideration in the communication filed on 17 May 2007 is acknowledged and the amendments are entered.

Claims 1-33 and 68-70 are pending, and claims 1-4, 8-9, 12-33 and 68-70 are examined in the instant Office action.

Allowable Subject Matter

Claim 33 is allowed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The following rejections are newly applied:

Claims 1-4, 8-9, 12-32 and 68-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4, 8-9, 12-32 and 68-70 consistently use the term "defined" with regards to biological activity or the degree of the defined biological activity. It is not known to whom, when and where these quantities are defined. Furthermore, the method steps do not recite any generic or specific biological activities.

Claim 70 uses the term "known PPAR-gamma partial agonist," where it is unclear to whom, when or where the agonist is known.

Claim Rejections - 35 USC § 101

The rejection of claim 33 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn due to amendments made on 17 May 2007.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following rejection is reiterated from the Office action of 17 January 2007 for claims 1-4, 8-9, and 12-32 and necessitated by amendment of applicant filed 17 May 2007 for claims 68-70:

Claims 1-4, 8-9, 12-32, and 68-70 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The following analysis of facts of this particular patent application follows the analysis suggested in the "Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility". Note that the text of the Guidelines is italicized.

To satisfy section 101 requirements, the claim must be for a practical application of the § 101 judicial exception, which can be identified in various ways (Guidelines, p. 19):

- The claimed invention "transforms" an article or physical object to a different state or thing.

- The claimed invention otherwise produces a useful, concrete and tangible result.

In the instant case, the claimed invention does not "transform" an article or physical object to a different state or thing because the instant set of claims of determining whether an agent possesses a biological activity does not result in a physical transformation. This does not preclude the subject matter to be patentable as, for eligibility analysis, as

physical transformation "is not an invariable requirement, but merely one example of how a mathematical algorithm [or law of nature] may bring about a useful application." AT&T, 172 F.3d at 1358-59, 50 USPQ2d at 1452. If the examiner determines that the claim does not entail the transformation of an article, then the examiner shall review the claim to determine if the claim provides a practical application that produces a useful, tangible and concrete result. In determining whether the claim is for a "practical application," the focus is not on whether the steps taken to achieve a particular result are useful, tangible and concrete, but rather that the final result achieved by the claimed invention is "useful, tangible and concrete." The claim must be examined to see if it includes anything more than a § 101 judicial exception. If the claim is directed to a practical application of the § 101 judicial exception producing a result tied to the physical world that does not preempt the judicial exception, then the claim meets the statutory requirement of 35 U.S.C. § 101. If the examiner does not find such a practical application, the examiner has determined that the claim is nonstatutory. (Guidelines, p. 20)

The question is thus whether the final result achieved by the claimed invention satisfies all three criteria of being useful, and concrete, and tangible.

Furthermore, the useful, tangible, and concrete result must be recited in the claim itself, rather than addressed in specification.

(2) **"TANGIBLE RESULT"** The tangible requirement does not necessarily mean that a claim must either be tied to a particular machine or apparatus or must operate to change articles or materials to a different state or thing. However, the tangible requirement does require that the claim must recite more than a § 101 judicial exception, in that the process claim must set forth a practical application of that § 101

judicial exception to produce a real-world result. The opposite meaning of "tangible" is "abstract."

The instant claims are drawn to computational means for determining whether an agent possesses a biological activity. However, as claimed, the method does not produce a tangible result. For example, the method as claimed may take place entirely within the confines of a computer or a human mind without any communication to the outside world and without using or making available for use, the results of the computation. Thus, the instant methods of the claims do not produce any tangible result.

Therefore, the final result achieved by the claimed invention does not satisfy all three criteria of being useful, and concrete, and tangible.

Response to Arguments

Applicant's arguments filed 17 May 2007 have been fully considered but they are not persuasive.

With regards to the arguments against the 35 U.S.C. 101 rejection on pages 12-13 of the Remarks of 17 May 2007, applicants argues that the amendment of adding step "a" to the independent claims introduces a physical transformation and therefore overcomes the rejections of record.

This argument (and amendment) does not overcome the rejection of record because this step of obtaining an expression measurement may be accomplished computationally on a database in which case the claim would not realize a physical transformation. Even if it were assumed that this step produces a physical

transformation, the transformation is not material to the outcome of the set of method steps. In other words, the output of the claimed method is not a physical transformation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 12-16, 18-26, 28, and 30-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Castle et al. [WO 02/059560 A2].

Claims 1-4, 12-16, 18-26, 28, and 30-32 state:

Claim 1 is drawn to a method for determining whether an agent possesses a defined biological activity, the method comprising the steps of:

-obtaining the expression measurement of at least one gene population or at least one protein population in living cells contacted with an agent and generating at least one of an efficacy value of the agent, a toxicity value of the agent or a classifier value of the agent,

- making at least one comparison selected from the group consisting of:

1) comparison of efficacy values with reference values

2) comparison of toxicity values with reference values

3) comparison of classifier values with reference values

- using the comparison results obtained in the previous step to determine whether the agent possesses the defined biological activity and determine the degree of the defined biological activity.

Claim 2 is drawn to the same subject matter as claim 1, except two comparisons are made from the list of three.

Claim 3 is drawn to the same subject matter as claim 1, except all three comparisons are made from the list of three.

Claim 4 is dependent from claim 1 with the extra limitation that the agent is a chemical agent.

Claim 12 is dependent from claim 1 with the extra limitation of the at least one reference classifier value is the classifier value of a reference agent that possesses the defined biological activity.

The document of Castle et al., studies a method and system for predicting the biological activity, including toxicology and toxicity, of substances, and states in the abstract:

> A method for assessing toxicity and toxicology of a substance is disclosed comprising: exposing a set of at least two genes to the substance; monitoring the response of each gene in the set of genes to the substances; analyzing the variance of the response to the substance for each gene using contrast analysis; constructing a summary score for each gene in the set of genes; performing a logistic regression analysis upon the summary scores; and using the results of the logistic regression analysis to provide a predictive model regarding the toxicity and toxicology of the substance.

The algorithm of interest is elaborated on pages 32-33 of Castle et al., which states:

> The following is a model developed from gene expression of rat livers using Affymetrix RU35 Rat Chip data. The rats were either treated with a toxic dose, non-toxic dose or vehicle controls. The raw expression data expressed as normalized average differences were then entered into the model described here.
>
> In achieving this analysis, a preferred expression similarity profiling for predictive toxicology algorithm is employed. In this algorithm, let Xij represent gene expression values for the i'th gene and j'th sample (I = 1 to I, j = 1 to J). Let Yj, Dj, and Tj represent the indicator of toxicity for the j'th sample, the dose for the j'th sample, and the time for the j'th sample, respectively. In the first step, time stable and dose dependent patterns are selected. For gene i,fit a two-factor analysis of variance model. This model can be expressed as
>
> Xij = a+b*Dj+c*Tj+d*Dj*Tj
>
> for the case of two dose groups (Dj = 0 or 1) and two time points (Tj = 0 or 1). In this model, the parameters (a, b, c, d) are estimated via a least squares algorithm.
> Accomodating additional time/dose levels is accomplished by adding additional model parameters for each additional time and/or dose level. For example, the case of four time points (Tj = 0 or 1 or 2 or 3) and three dose groups (Dj = 0 or 1 or 2 can be expressed as:
>
> Xij = a+B1*D1j+b2*D2j+c1*T1j+c2*t2j+c3*t3j+d1*D1j*T1j+ d2*D1j*T2j+ d3*D1j*T3j+ d4*D2j*T1j+d5*D1j*T2j+d6*D2j*T3j
>
> Where T1j = 1 if Tj = 1, T2j = 1 if Tj = 2, etc. The parameters (a, b1, b2, c1, c2, c3, d1, d2, d3, d4, d5, d6) are estimated as above.

Consequently, Castle et al. use linear regression to compare the reference toxicity of a substance (toxicity of a chemical agent at an initial time) to toxicity as time progresses. Although this passage describes nominally a toxicological algorithm, the actual algorithm itself is not limited to toxicology. As stated in page 8, line 10-17:

> An aspect of the present invention is an analysis of the variance for each gene contrast analysis. In this gene contrast analysis, the response of a gene or set of genes is monitored upon exposure to a chemical. In one preferred embodiment, the response of a gene or set of genes to a chemical can be fitted into one of four patterns illustrated in Figures 1a, 1b, 1c, and 1d. In this preferred embodiment, upon classification into one of these four groups, an analysis is then performed which categorizes the gene contrast analysis as one of four summary scores...

Figure 1 of Castle et al. is interpreted to illustrate a) efficacy, b) toxicity, c) no effect, or d) plateau effect of the agent. The model of Castle et al. is used not only to determine agent toxicity, but also agent efficacy, by assigning the agent a classification such as that shown in Figure 1 of Castle et al. The reference value is interpreted to be the effect of the agent at an initial time on the set of genes while the actual value is interpreted to be the efficacy, toxicity, or classification of the agent at the final time

examined. The effect on gene expression caused by the agent determines the classification of biological activity of the agent. The instant disclosure does not limit the relation between the reference and actual agents to possess a specific relationship in time (i.e. the reference and actual samples are interpreted to occur at different times on the same tissue sample).

Claim 13 is dependent from claim 1 wherein at least one member of the group consisting of the efficacy value of the agent, the toxicity value of the agent and the classifier value of the agent is calculated and measured from in vitro data and procedures.

Claim 14 is dependent from claim 13 wherein at least two members of the group consisting of the efficacy value of the agent, the toxicity value of the agent and the classifier value of the agent are calculated and measured from in vitro data and procedures.

Claim 15 is dependent from claim 13 wherein all of the members of the group consisting of the efficacy value of the agent, the toxicity value of the agent and the classifier value of the agent are calculated and measured from in vitro data and procedures.

Claim 16 is dependent from claim 13 wherein the living cells are selected from the group consisting of heart cells, liver cells and adipocyte cells.

The analysis completed is Castle et al. in completed on a chip *in vitro* on rat liver cells to analyze gene expression related to disease. The purpose of the study of Castle

et al. is to predict the effect of substances *in vivo* as a result of *in vitro* experimentation. Castle et al. use a plurality of different tissue samples in the Affymetrix gene chip to complete the analysis (there are a plurality of tissue samples or "j's" in the equations listed). Each tissue sample affects the linear regression analysis (i.e. calculations) of the equations cited above in Castle et al. Each tissue sample "j" is interpreted to be its own tissue type, wherein each tissue type affects one another in the computation of agent efficacy or toxicity.

Claim 28 is dependent from claim 1 with the additional limitation that at least one member of the group consisting of the toxicity-related population of genes and the toxicity-related population of proteins yields at least one toxicity-related gene expression pattern, or toxicity-related protein expression pattern, in response to the agent, that correlates with the presence of at least one undesirable response caused by the agent in the living thing, wherein the at least one toxicity-related gene expression pattern, or at least one toxicity-related protein expression pattern, appears before the undesirable biological response.

Claim 30 is dependent from claim 1 with the additional limitations of comparing at least one of efficacy values to a scale of efficacy values, toxicity values to a scale of toxicity values, a classifier value to a scale of classifier values and using comparison results to determine possession of biological activity.

Claim 31 is dependent from claim 1 with the additional limitations of comparing at least two of efficacy values to a scale of efficacy values, toxicity values to a scale of

toxicity values, a classifier value to a scale of classifier values and using comparison results to determine possession of biological activity.

Claim 32 is dependent from claim 1 with the additional limitations of comparing efficacy values to a scale of efficacy values, toxicity values to a scale of toxicity values, a classifier value to a scale of classifier values and using comparison results to determine possession of biological activity.

Castle et al. use linear regression to compare the reference toxicity of a substance (toxicity of a chemical agent at an initial time) to toxicity as time progresses. Although this passage describes nominally a toxicological algorithm, the actual algorithm itself is not limited to toxicology. As stated in page 8, line 10-17:

> An aspect of the present invention is an analysis of the variance for each gene contrast analysis. In this gene contrast analysis, the response of a gene or set of genes is monitored upon exposure to a chemical. In one preferred embodiment, the response of a gene or set of genes to a chemical can be fitted into one of four patterns illustrated in Figures 1a, 1b, 1c, and 1d. In this preferred embodiment, upon classification into one of these four groups, an analysis is then performed which categorizes the gene contrast analysis as one of four summary scores...

Figure 1 of Castle et al. is interpreted to illustrate a) efficacy, b) toxicity, c) no effect, or d) plateau effect of the agent. The model of Castle et al. is used not only to determine agent toxicity, but also agent efficacy, by assigning the agent a classification such as that shown in Figure 1 of Castle et al. The scaling value is interpreted to be the effect of the agent at an initial time on the set of genes while the actual value is interpreted to be the efficacy, toxicity, or classification of the agent at the final time examined. The effect on gene expression caused by the agent determines the classification of biological activity of the agent. The instant disclosure does not limit the relation between the reference and actual agents to possess a specific relationship in

time (i.e. the reference and actual samples are interpreted to occur at different times on the same tissue sample).

Response to Arguments

Applicant's arguments filed 17 May 2007 have been fully considered but they are not persuasive.

With regards to the arguments against the 35 U.S.C. 102(b) rejection on pages 13-14 of the Remarks of 17 May 2007, applicant attempts to first overcome the rejection by amending the independent claims to determine the degree of the "defined" biological activity. This is not found to be persuasive because this amendment does not further limit the claim; in fact, it broadens and makes the claim indefinite (see 35 U.S.C. 112 section) because it is no known to whom, when and where the biological activity is defined.

Applicant next argues on pages 13-14 of the Remarks of 17 May 2007 that the logistic regression analysis deals with a binary categorical outcome rather than a continuous outcome as applicant described in the instant specification. This argument is not found to be persuasive because the limitation of a continuous outcome, while present in the original specification, is not present in the instant set of claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 8, 9, 17, 27, 29, and 68-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Castle et al. as applied to claims 1-4, 12-16, 18-26, 28, and 30-32 above in further view of Mukherjee et al. [Molecular Endocrinology, 2000, volume 14, pages 1425-1433].

Claim 8 is dependent from claim 1 with the additional limitation that the defined biological activity is partial agonist activity with respect to a biological response, or with respect to a protein that mediates a biological response.

Claim 9 is dependent from claim 8 with the additional limitation that the defined biological activity is partial agonist activity with respect to PPAR-gamma.

Claim 17 is dependent from claim 16 with the additional limitation that the living cells are 3T3L1 adipocyte cells.

Claims 27 and 29 are both dependent from claim 1 with the further limitation of requiring gene and protein expression patterns.

Castle et al. does not teach partial agonist activity with respect to a biological response, partial agonist activity with respect to PPAR-gamma, use of 3T3L1 adipocyte cells, or production of an efficacy related gene pattern.

The article of Mukherjee et al. studies the selective peroxisome proliferator-activated receptor-gamma (PPAR-gamma) modulator blocking adipocyte differentiation but stimulates glucose uptake in 3T3-L1 adipocytes, and states in the abstract:

> Peroxisome proliferator-activated receptor-gamma (PPAR-gamma) agonists such as the thiazolidinediones are insulin sensitizers used in the treatment of type 2 diabetes. These compounds induce adipogenesis in cell culture models and increase weight gain in rodents and humans. We have identified a novel PPAR-gamma ligand, LG100641, that does not activate PPAR-gamma but selectively and competitively blocks thiazolidinedione-induced PPAR-gamma activation and adipocyte conversion. It also antagonizes target gene activation as well as repression in agonist-treated 3T3-L1 adipocytes.

The first paragraph in the introduction of Mukherjee et al. elaborates on the scope and purpose of the study:

> Peroxisome proliferator-activated receptor-gamma (PPAR-gamma) is a member of the intracellular receptor family of transcription factors... PPAR-gamma) is expressed at high levels in fat, spleen, and colon but is also detectable in skeletal muscle, liver and other tissues... Interest in this receptor increased when it was clear that insulin sensitizers of the thiazolidinedione class [troglitazone, rosiglitazone (BRL 49653), Pioglitazone], are high-affinity ligands for PPAR-gamma. A correlation was reported between the affinity of thiazolidinediones for PPAR-gamma and the minimum effective dose required to lower glucose levels in diabetic rodent models.

Consequently, there is a correlation between PPAR-gamma affinity and the lowering of glucose in diabetic rodent models.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the toxicological algorithm of Castle et al. as applied to

claims 1-4, 12-16, 18-26, 28, and 30-32 above to determine and classify the activity of an agent by use of the PPAR-gamma efficacy analysis of Mukherjee et al. because while both studies examine rodent cells, Mukherjee et al. has the advantage of exemplifying a correlation of the relations between the required agents, cell species, and the efficacy in treating diabetes related complications.

Claim 68 is drawn to a method for determining whether an agent possesses agonist activity with respect to a defined biological response, or with respect to a protein that mediates a defined biological response, comprising the steps of:

-- obtaining an expression measurement of at least one gene population or at least one protein population in living cells contacted with an agent and generating an efficacy value of the agent and a toxicity value of the agent:

-- comparing the efficacy value of the agent to at least one reference efficacy value to yield an efficacy comparison result, wherein each efficacy value represents at least one expression pattern of the same efficacy-related population of genes, or at least one expression pattern of the same efficacy-related population of proteins,

-- comparing the toxicity value of the agent to: a reference agonist value to yield a agonist toxicity comparison result and a reference partial agonist value, wherein each agonist toxicity value and partial agonist value represents at least one expression pattern of the same toxicity-related population of genes that distinguish between the agonist and the partial agonist, or at least one expression pattern of the same toxicity-related population of proteins, and

-- using the comparison results obtained above to select agents that possesses a desired degree of agonist activity with respect to biological response, or with respect to a protein that mediates a biological response.

Claim 69 is dependent from claim 68 with the additional limitation that the biological response is partial agonist activity with respect to PPAR-gamma.

Claim 70 is dependent from claim 69 with the additional limitation that the reference partial agonist toxicity value is generated using a known PPAR-gamma partial agonist toxicity value.

Castle et al. as applied to claims 1-4, 12-16, 18-26, 28, and 30-32 above does not teach partial toxicity values in order to analyze agent toxicologies.

The article of Mukherjee et al. studies the selective peroxisome prolierator-activated receptor-gamma (PPAR-gamma) modulator blocking adipocyte differentiation but stimulates glucose uptake in 3T3-L1 adipocytes, and states in the abstract:

> Peroxisome proliferator-activated receptor-gamma (PPAR-gamma) agonists such as the thiazolidinediones are insulin sensitizers used in the treatment of type 2 diabetes. These compounds induce adipogenesis in cell culture models and increase weight gain in rodents and humans. We have identified a novel PPAR-gamma ligand, LG100641, that does not activate PPAR-gamma but selectively and competitively blocks thiazolidinedione-induced PPAR-gamma activation and adipocyte conversion. It also antagonizes target gene activation as well as repression in agonist-treated 3T3-L1 adipocytes.

The first paragraph in the introduction of Mukherjee et al. elaborates on the scope and purpose of the study:

> Peroxisome proliferator-activated receptor-gamma (PPAR-gamma) is a member of the intracellular receptor family of transcription factors... PPAR-gamma) is expressed at high levels in fat, spleen, and colon but is also detectable in skeletal muscle, liver and other tissues... Interest in this receptor increased when it was clear that insulin sensitizers of the thiazolidinedione class [troglitazone, rosiglitazone (BRL 49653), Pioglitazone], are high-affinity ligands for PPAR-gamma. A correlation was reported between the affinity of thiazolidinediones for PPAR-gamma and the minimum effective dose required to lower glucose levels in diabetic rodent models.

Consequently, there is a correlation between PPAR-gamma affinity and the lowering of glucose in diabetic rodent models.

While the combination of Castle et al. and Mukherjee et al., taken as a whole, teach all of the required elements of the instantly rejected claims, the rationale to combine the two sources is because the substitutions of PPAR-gamma in Mukherjee et al. for the generic substances of Castle et al. would obtain predictable results analogous to those of Mukherjee et al. for diabetes. [see KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (2007)].

Response to Arguments

Applicant's arguments filed 17 May 2007 have been fully considered but they are not persuasive.

With regards to the arguments against the 35 U.S.C. 103(a) rejection on pages 15-18 of the Remarks of 17 May 2007, applicant has four bases for arguments against this obviousness prior art rejection.

First, applicant argues that due to the inadequacies of the Castle et al. reference in discussing continuous degrees of biological activity this rejection should be withdrawn. This is not found to be persuasive because of the reasons discussed above with regards to the anticipatory prior art rejection.

Second, applicant argues that Castle et al. fails to teach of suggest the determination of an efficacy values or a classifier value of an agent, and focuses on

toxicology. Applicant argues that Figure 1 of Castle et al. is insufficient in discussing efficacy and classification and the Figures themselves are insufficient due to lack of axes labels.

This argument is not found to be persuasive for several reasons. First, in the Remarks, applicant sites page 8, lines 10-17 of Castle et al., within which it is stated:

> In one preferred embodiment, the response of gene or set of genes to a chemical can be fitted into one or four patterns illustrates in Figures 1a, 1b, 1c, and 1d.

Consequently, applicant is admitting in the arguments that a classification occurs and is scored.

Furthermore, the caption of Figure 1 on page 7 (lines 12-13) of Castle et al. states:

> Figures 1a, 1b, 1c, and 1d present four preferred patterns for illustrating the response of a gene or set of genes to a chemical.

Consequently, the term "response" indicates an inherent property of the Figure that the x-axis is based on a time related property. Each response indicates an overexpression, underexpression, or plateau effect of the chemical on a gene. While one of the responses for each gene is construed as a toxic response, the opposite response is construed as effective.

Third, applicant agrees with the conclusion in the previous Office action that the study of Castle et al. does not teach PPAR-gamma or a gene related pattern. This argument is found to be persuasive as in the rationale for use of the Mukherjee et al. reference.

Fourth, applicant argues against the motivation to combine the Castle et al. reference and the Mukherjee et al. reference. This is not found to be persuasive for

several reasons. First, Castle et al. and Mukherjee et al. teach analogous problems of applying a agent to gene expression and the study of toxicity. Mukherjee et al. teaches a species of chemicals (including PPAR-gamma) to which the study of Castle et al. can be utilized. In light of the recent Supreme Court decision of KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (2007), it would be obvious to use simple substitution of the species of Mukherjee et al. (PPAR-gamma) with predictable results to the study of Castle et al. to result in the claimed invention. It should be noted that the recent Supreme Court decision of KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (2007) forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness.

Conclusion

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Ram Shukla, Supervisory Patent Examiner, can be reached at (571) 272-0735.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

7/16/07

/Shubo (Joe) Zhou/

RSN
26 July 2007

SHUBO (JOE) ZHOU, PH.D.
PRIMARY EXAMINER